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09/576,057	05/23/2000	Joseph Chappell	07678-011004	3528

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EXAMINER
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ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/576,057	Applicant(s) Chappell et al.
	Examiner Nashaat T. Nashed	Art Unit 1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *Jun 17, 2002*.

2a) [ ] This action is **FINAL.** 2b) [X] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *1-14* is/are pending in the application.

4a) Of the above, claim(s) *10-14* is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *1-9* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [X] The drawing(s) filed on *May 23, 2000* is/are a) [X] accepted or b) [ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____.
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) [ ] The translation of the foreign language provisional application has been received.

15) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [X] Notice of References Cited (PTO-892)
2) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) [X] Information Disclosure Statement(s) (PTO-1449) Paper No(s). *3*
4) [ ] Interview Summary (PTO-413) Paper No(s). _____
5) [ ] Notice of Informal Patent Application (PTO-152)
6) [ ] Other

Applicant's election with traverse of Group I (claims 1-9, the tobacco-*Hyoscyamus* CH4 chimeric isoprenoid synthase) in Paper No. is acknowledged. The traversal is on the ground(s) that all the claims are generic and examining them together does not represent a search burden on the examiner. This is not found persuasive in part because claims 1-9 are directed to chimeric polypeptide, whereas claims 10-14 are directed to nucleic acid molecule, vectors, and host cells. The nucleic acids and the polypeptides are independent chemical entities and require separate searches in the patent and non-patent literature. On the other hand, the argument regarding the chimeric proteins: CH4, CH10, CH11, CH12, CH13, and CH14 is considered reasonable since all said chimeric proteins are derived from the same two proteins. Said chimeric protein are considered different species of the same invention. Therefore, the elected species for initial prosecution is the CH4 chimeric protein.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-9 are under consideration. The elected species for initial prosecution is tobacco-*Hyoscyamus* CH4 chimeric isoprenoid synthase.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. The application discloses nucleic acid and/or protein sequences shown in Figure 4A without their sequences being in the sequence listing or the Computer Readable Form (CRF). Also, there are several references to specific amino acid residues, presumably, from a specific amino acid sequence without having the amino acid sequence listed in the sequence listing, the CRF, and identification of the amino acid sequence with a sequence identification number, see for example Table 1 on page 16. Applicant reliance on a restriction sites map for TEAS and HVS is insufficient to illustrate the structure of their invention. The restriction map may differ in allelic variants of the same gene from the same biological source. Without identifying the nucleic acid sequences and the corresponding amino acid sequences, one of ordinary skill in the art would not be able to reproduce the claimed invention. Applicants are required to comply with the sequence rule by filing a new sequence listing, CRF, and an amendment to delete the paper copy of the sequence listing and enter the new one along with a statement indicating that the CRF and the paper copy of the sequence listing are identical and contain no new matter.

Claim 6 is objected to under 37 CFR § 1.75(d)(1) as being in improper form because the claim states an improper Markush groups. Compounds included within a Markush

group must "(1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility." (See MPEP § 803.02.). The various members of the Markush group in the claims are different chemical compound and do not share a common structural feature required for the stated utility and in many cases do not share the same utility.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-9 are directed to all possible combinations of chimeric isoprenoid synthase catalyzing any cyclization reaction involving geranyl diphosphate, farnesyl diphosphate, geranylgeranyl diphosphate or any other natural or man made related structure. The specification, however, only provides a single representative species encompassed by these claims involving plant tobacco TEAS and *Hyoscymaus* HVS genes. Without even identifying or teaching said genes in the specification, applicant cut and pasted the two genes together using restriction enzymes. Applicants was successful not in producing new compounds or enzymatic activities, but rather in producing an enzyme lacking product selectivity, a highly undesirable results. No new compound of any kind is reported, let alone those having any of the activities cited in claims 7-9. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species whereby one of ordinary skill in the art would be able to design and recruit new desired enzymatic activities which enable the biosynthesis of new and useful compounds as the applicants suggested in the specification. The specification failed to provide any structural units of these enzymes from plants, let alone those from mammals, bacteria and fungus. Claim 6 is directed to a specific chemical compound having no structure and one of ordinary skill in the art would not be able to re-construct them by the teaching of the specification. The structure of the starting genes are not defined in the specification, and isolating the genes from their natural source probably would provide allelic variants which may have different restriction sites. Thus, one of ordinary skill in the art would not be able to reproduce the tobacco-*Hyscyamus* CH4 chimeric isoprenoid synthase described in the specification. The specification also fails to describe additional representative species of these chimeric

isoprenoid synthases by any identifying structural characteristics or properties other than their ability of producing isoprenoid product that is not formed in the absence of the second isoprenoid synthase, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Claims 1-9 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to chimeric synthase produced by cutting and pasting the tobacco TEAS and *Hyoscymaus* HVS genes provided that the applicant correct the deficiencies described above. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to the huge number of all possible chimeric isoprenoid synthases as defined by the specification. Factors to be considered in determining whether undue experimentation is required, are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses any chimeric isoprenoid synthases comprising two polypeptides from two different synthases including the full length synthases, variants and mutants thereof that include insertion, deletion substitution and combination thereof. The specification provides guidance and examples in the form of an assay to make the chimeric proteins shown in Figure 4 from, presumably, known plant genes that lost their specificity in product formation. While molecular biological techniques and genetic manipulation to make and claimed chimeric proteins are known in the prior art and the skill of the artisan are well developed, knowledge of the catalytic and specificity domains for synthases from various biological sources including plants, mammals, bacteria and fungus, how to engineer a desired substrate specificity in isoprenoid synthases, and engineering a specificity for product formation is lacking. Thus, searching for a chimeric isoprenoid synthase which is able to accept and catalyzes the formation of a desired product is well outside the realm of routine experimentation and predictability in the art of success is extremely low. The amount of experimentation to identify a chimeric protein capable of catalyzing specific transformation in is enormous. Since routine experimentation in the art does not include screening vast numbers of chimeric synthase where the expectation of obtaining the desired synthase is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the structure bases for the substrate and product

specificities, the identification of various structural elements in various isoprenoid synthases, the conservation of various structural elements of isoprenoid synthases among plants, bacteria, fungus, and mammals. Without such a guidance, the experimentation left to those skilled in the art is undue.

Claims 1-9 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

(a) The phrase "comprising a first isoprenoid synthase polypeptide joined to a second, different isoprenoid synthase polypeptide" in claim 1 render the claim indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. The claim is confusing because it has at least two meaning. One of the possible meaning is one full length isoprenoid synthase is fused to another full length isoprenoid synthase. A second possible meaning is that a fragment of a first is fused to complementary fragment of another isoprenoid synthase. For examination purposes only the phrase is taken to mean any polypeptide from first synthase including the full length fused to another polypeptide from a second synthase including the full length.

(b) The phrases "catalyzes at least two different isoprenoid reaction products" in claim 4 and "tobacco-*Hyoscyamus* CH4 chimeric isoprenoid synthase" in claims 6 render the claims indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. For examination purposes, the phrases "catalyzes at least two different isoprenoid reaction products" is assumed to mean "catalyzes the formation of at least two different isoprenoid products". The phrase "tobacco-*Hyoscyamus* CH4 chimeric isoprenoid synthase" is not defined in the specification by a specific structure and one of ordinary skill in the art would not know its structure. For examination purposes, the phrase is taken to mean a chimeric isoprenoid synthase constructed from any fragments of the synthase from tobacco and *Hyoscyamus*.

(c) the phrase "the production of antifungal agent" in claim 7, "the production of an antibacterial agent" in claim 8, and the production of antitumor agent" in claim 9 render the claims indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. The specification does not provide teachings of any antifungal, antibacterial or anticancer compounds, and one of ordinary skill in the art would not know what they are. For examination purposes only, the phrase is taken to mean novel compounds.

(d) claims 2, 3, and 5 are included in these rejection because they are dependent on rejected claims and do not cure its deficiencies.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-5 and 7-9 are rejected under 35 U.S.C. 102(e) as being anticipated by 5,744,341 ('341, Cunningham *et al.*).

The '341 patent teaches two isoprenoid synthase named β-cyclase and ε-cyclase form *Arabidopsis thaliana*, see Figure 13. They teach the formation of chimeric cyclase by replacing homologous regions in one gene by another and thereby, produce an enzyme with novel function, characteristic and products (claims 1-5 and 7-9), see column 5, lines 40-55.

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 6 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 5 of prior U.S. Patent No. 5,824,774. This is a double patenting rejection.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4 and 7-9 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 and 15-18 of U.S. Patent No. 5,824,774 ('774). Although the conflicting claims are not identical, they are not patentably distinct from each other because the embodiment of the claims in the '774 are encompassed by the claims of the instant application. Claim 1 of the instant application from which all other claims are dependent is drawn to any chimeric protein comprising a polypeptides from two isoprenoid synthase including the full length isoprenoid synthase which encompasses the more narrower embodiment of claim 1 of the '774 patent.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is (703) 305-6586. The examiner can normally be reached Monday, Tuesday, Thursday, and Friday from 9:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (703) 308-3804. The fax phone numbers for this Group are (703) 305-3014 and (703)308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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Primary Examiner

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